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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,527	10/29/2003	Zhelong Xu	USAV2001/0092 US CNT	6385

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 12/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/696,527	XU ET AL.	
	Examiner	Art Unit	
	Yong S. Chong	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 11/1/2005. Claims 1, 4, 9 have been amended. Claims 1-15 are pending and are examined herein.

Response to Arguments

Applicant's arguments have been fully considered and found persuasive enough to withdraw all of the rejections in the last Office Action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-11, 13, 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Smits et al. ("Cardioprotective effects of the novel adenosine A1/A2 receptor agonist AMP 579 in a porcine model of myocardial infarction." *Journal of Pharmacology and Experimental Therapeutics*, vol. 286, no. 2, August 1998, pgs. 611-618).

Smits et al. teach the cardioprotective effects of AMP 579, an A1/A2 receptor agonist, in a model of myocardial infarction, which was induced by a 40 min occlusion of the left anterior descending coronary artery, followed by 3 h of reperfusion. In one particular experiment, AMP 579 (3μg/kg i.v.) was administered 30 min after the onset of myocardial ischemia, 10 min before reperfusion through 1 hr of reperfusion (abstract).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-8, 12, 14 are rejected under 35 U.S.C. 103(a) as being obvious over Smits et al. ("Cardioprotective effects of the novel adenosine A1/A2 receptor agonist AMP 579 in a porcine model of myocardial infarction." *Journal of Pharmacology and Experimental Therapeutics*, vol. 286, no. 2, August 1998, pgs. 611-618) as applied to claims 9-11, 13, 15 in view of Berge et al. ("Pharmaceutical Salts" *Journal of Pharmaceutical Sciences*, vol. 66, no. 1, January 1977).

The instant claims are directed to a method of providing cardioprotection with a compound having adenosine A1/A2 agonist activity, beginning at a time 10 minutes before and after the onset of reperfusion, and continuing for a period of more than 30 min after onset of reperfusion.

Smits et al. teach as discussed above. What's more, it would have been obvious to one of ordinary skill in the art to optimize the not only the start time for administration but also the length of time AMP 579 is administered to a patient. Applicant is required to supply evidence why a start time of 10 min after the onset of reperfusion is unexpecting and unobvious over a start time of 10 min before the onset of reperfusion, in addition to the longer duration of treatment from 60 min to 70 min after the onset of reperfusion.

Generally, mere optimization of ranges will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "When the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimal or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also *In re Peterson*, 315 F. 3d at 1330, 65 USPQ 2d at 1382 "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." MPEP 2114.04.

However, Smits et al. fail to disclose a pharmaceutical acceptable salt form of the A1/A2 agonistic compound.

Berge et al. teach that it's widely known to those in the art to convert drugs into their salt form (pg. 1, paragraph 1). The salt form is known to improve many properties such as dissolution rate, solubility, and stability (pg. 5, paragraphs 3-4). Thus, enhanced solubility results in improved bioavailability (pg. 10, paragraph 11-12).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to administer the adenosine A1/A2 agonistic compound in a pharmaceutically acceptable salt form because of the expectancy of increased solubility of the compound in a pharmaceutically acceptable carrier.

A person of ordinary skill in the art would have been motivated to formulate the adenosine A1/A2 agonistic compound in a pharmaceutically acceptable salt form because of the expectancy of increasing the bioavailability and efficacy of the compound in the patient according to Berge et al.

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being obvious over Clark et al. (Cardiovascular Drug Reviews, vol. 18, no.3, 2000, pages 183-210) and further in view of Berge et al. (Berge SM, Bighley LD, Monkhouse DC. "Pharmaceutical Salts" *Journal of Pharmaceutical Sciences*, vol. 66, no. 1, January 1977).

The instant claims are as stated above.

Clark et al. teach that AMP 579 is a novel adenosine A1/A2 receptor agonist with significant potential to pharmacologically induce cardioprotection during myocardial infarction and cardiac surgery (pg. 184, paragraph 4). Intravenous AMP 579 showed striking cardioprotection in pigs when administered through the first hour of reperfusion (pg. 188, paragraph 2). Furthermore, a similar magnitude of cardioprotection is observed when AMP 579 is administered 20 minutes after the onset of myocardial ischemia and 10 minutes prior to the onset of reperfusion (pg. 191, paragraph 2). Furthermore, Clark et al. teach that administration of AMP 579 can by given up to 6

hours, constant rate infusion in a patient (pg. 201, paragraph 1). It would have been obvious to one of ordinary skill in the art to optimize the not only the start time for administration but also the length of time AMP 579 is administered to a patient.

Generally, mere optimization of ranges will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "When the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimal or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also *In re Peterson*, 315 F. 3d at 1330, 65 USPQ 2d at 1382 "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." MPEP 2114.04.

However, Clark et al. fail to disclose a pharmaceutical acceptable salt form of the A1/A2 agonistic compound.

Berge et al. teach as discussed above.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to administer the adenosine A1/A2 agonistic compound in a pharmaceutically acceptable salt form because of the expectancy of increased solubility of the compound in a pharmaceutically acceptable carrier.

A person of ordinary skill in the art would have been motivated to formulate the adenosine A1/A2 agonistic compound in a pharmaceutically acceptable salt form

because of the expectancy of increasing the bioavailability and efficacy of the compound in the patient according to Berge et al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHENGJUN WANG
PRIMARY EXAMINER

YSC